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TOPICAL COMPOSITION IN THE FORM OF A GEL FOR ~~THE~~ TREATING ~~MENT OF~~ SKIN BURNS

FIELD OF THE INVENTION

The present invention relates to a novel topical ~~topical~~ compositions for the local treatment of burns, abrasions~~grazes~~, erythema, ecz~~e~~ema, herpectic~~s~~ infections, aevulsions ~~surface sores~~ and any sphacelus causing skin injury ~~damage leading to gangrene~~ and ~~in~~ particularly ~~,~~ to a composition which forms a clear ~~creating a translucid~~ colloidal film over~~n~~ the injury covering the nerve endings~~ous terminals~~ (pain relief), reducing nerve~~ous~~ irritation~~bility~~, insulating if ~~isolating~~ from the surrounding environment to avoid~~external media preventing from~~ contact with harmful~~noxious~~ substances, and the ~~maintaining dryness of~~ injury dry and exerting ~~doing~~ pressure (dressing effect) to create a medium that will enable fast and effective cell regeneration~~for creating a media permitting effective and fast cell regeneration;~~ , while the enzymatic effect ~~action~~ reduces ~~causes des~~-inflammation, debrides and cleans ~~ing and cleaning~~ the zone.

BACKGROUND OF THE INVENTION

MEDICAL AND CLINICAL ENVIRONMENT

Traumatic injuries of skin, such as ~~i.e.,~~ burns, scalds, abrasions, ~~a~~evulsions, etc., have been studied and treated by the specialized branch of medicine of plastic surgery, involved in the issue under a ~~addressed to the theme, with~~ scientific perspective and in related researches.

Reconstructive and burn surgery ~~of burned people~~, an applied science being part of the ~~forming part of the~~ plastic surgery specialty~~ization~~, is a field where a ~~n area wherein a~~ specialized physician endeavors to ~~works~~ re-construct ~~ing~~ tissues, treat~~ing~~ burns and repairing ~~lost~~ skin layers when lost.

In the case of superficial ~~rface~~ skin injuries and burns, despite a well-known ~~although its~~ physiopathology, there has not been and there still is not, at the beginning of the XXI century ~~is clearly known, even beginning twenty one century there is no~~ a general consensus as to the ~~in~~ treatment of same, thus evidencing the lack of a deeper understanding of ~~showing deep ignorance in this~~ issue, while a great number of physicians act empirically or based on ~~and a big part of physicians guides in an empiric form or by~~ very basic information.

This situation has led to the sale, application and prescription as treatment ~~caused that~~ in this field of medicine of a wide variety of ~~an enormous number of~~ products having ~~of~~ different sources, from home-made preparations, herbs, ~~origin be applied, sold or indicate as a treatment, from empiric substances, plants~~, coffee, albumen~~white of an egg~~, Aloe vera, mucilage, etc., to~~until~~ tannins, mercurial preparations ~~y~~ and topical antibiotics. The above is the breadth ~~are the king~~ of

substances used for treating skin injuries due to ~~for~~ burns (or abrasions), which ~~firther~~ further shows the absence of unanimous consensus in this respect. ~~demonstrating lack of only one view.~~

The focus of such methods has commonly become a~~A~~ntibiotic and cicatrization therapy employing a wide variety of substances, among which we find ~~healing methods of therapy have a popular focus with variety of substances being more notorious~~ sulfas, furazolidone, tetracycline, gentamici~~y~~n~~e~~, mercurochrome~~y-chrome~~, epithelial growing factor and tannins, whose effects have been studied and are well~~with studied and~~ known ~~results~~. However, the treatment of the main symptoms~~local treatment of principal symptoms~~ (pain, inflammation, debriding effect) in a local form has not received any substantial ~~has no received important~~ pharmacological attention.

Antibiotic substances such as silver sulfadiazine, furacine (fucidin), terramy~~i~~ci~~y~~n and other types of substances ~~hace~~have tried to fill this gap in ~~of different type have treated to occupy this space of~~ medical therapeutics.

Unquestionably, s~~S~~ilver sulfadiazine has enjoyed a greater success and has acquired a bigger market share~~is more successful and has bigger market~~. However, from a scientific viewpoint, it is a product far from perfect for treating ~~ally speaking, it is an imperfect product to manage~~ non-infected skin injuries.

The underlying ~~basic~~ concept is ~~considers~~ that the~~i~~s~~e~~ injuries heale~~d~~ by themselves ~~itself~~ (epithelializatio~~n~~e), regardless of the substance used~~with no~~

~~importance of the substance used~~, provided no ~~whenever~~ complications ~~do not~~ arise.

The object is thus to make ~~Philosophy is producing comfort to~~ the patient as comfortable as possible while his/her own body undergoes the cicatrization process. ~~while organism generates cicatrisation process by itself.~~

BURNS AND A~~E~~VULSIONS

A b~~B~~urn is defined as the ~~a~~ skin injury sustained from the ~~produced by energy~~ transfer of energy~~,~~ from a thermal~~o~~ source to the body which is large ~~, highly~~ enough to cause injury and which may result from~~, possibly by~~ direct conduction~~transmission~~ (heat~~caloric~~), chemical injury or electromagnetic radiation (electrical).

Immediate clinic manifestations of a ~~in~~ burn are changes in skin color from erythema to necrosis, intense~~deep~~ pain in surperficial ~~face~~ cases and presence of bodily fluids by transudation~~organic liquids by transweated~~.

A b~~B~~urn occurs ~~arises~~ when skin cells are destroyed by heat, thereby liberating nerve stimulating ~~chemical~~ chemical substances that cause ~~stimulating nerves causing~~ pain, producing the disruption of the ~~generating~~ skin and exposing the ~~continuity loss with~~ underlying elements ~~exposition~~ and, depending on the deepth ~~level~~, loss ~~loos~~ of fluids ~~liquid loss~~ by evaporation.

The ~~Burn~~ healing mechanism of a burn is similar to that of a wound or abrasion, in second degree burns, serum blisters ~~pimples~~ are formed that act~~ing~~ as a protective cover while underneath it ~~forming~~ a new skin layer is being formed from the sides of ~~under them from~~ the burn ~~boundaries~~.

If a burn is too big or remains ~~and~~ exposed, it becomes ~~is~~ easier for bacteria to enter the body.

Accordingly there are ~~s a consequence~~ many factors that come into play such as ~~the continuity~~ skin disruption~~loss~~, necrosis (death~~d~~) of the affected skin sector ~~affected~~, severe ~~deep~~ pain, the body's hydro-electrolitic response ~~of the organism~~, inflammation due to presence of fluids ~~by liquids~~ and chemicals, blushing due to ~~by~~ vasodilatation and the subsequent ~~further~~ possibility of bacterial colonization.

Likewise, ~~In~~ the ~~same way~~ defense mechanisms against hea~~o~~t are brought into action: profuse perspiration for lowering the ~~is bringing into play, abundant sweating to bring down~~ temperature by evaporation with ~~liquid~~ loss of fluids, heat~~ot~~ dissipation by vasodilation and ~~tissue~~ resistance of tissues to the heat ~~hot~~ or radiation (mainly ~~principally~~ muscles and skin, nerves and vessels are very sensitive). It is considered that no cell damage occurs at temperatures of up to ~~until~~ 44°C ~~no cell injury arises~~ unless there is very ~~of a~~ prolonged exposition.

EPIDEMIOLOGY

Burns are some the most ~~is one of the more~~ frequent injuries experienced by ~~occurring to~~ human beings. In the United States from~~about~~ 3.5 to 4 million people go the doctor for ~~visit physicians for~~ diagnostic~~is~~ and treatment of burns.

Burns account for a large ~~occupy a big~~ percentage of visits to emergency rooms and physician's offices~~medical consultation in hospitals and consulting rooms~~, 8 out of 10 persons experience a burn of some sort every ~~has some type of burn during a~~ year, being 95% of all burns subject to ~~of~~ home or ambulatory treatment ~~manage~~.

After a burn occurs and there is ~~In the moment of a burn dead~~ cell death, a ~~occurs, an event~~ series of events starts that bears some resemblance to that of ~~similar to~~ wounds ~~begin~~:

1- Inflammation: is the normal acute reaction of tissues after injury, immediate response is vasoconstriction by nervous stimulus and thrombosis.

2- Subsequently, there is ~~Follows a~~ vasodilatation and increase in ~~the~~ capillary permeability during ~~in~~ the following ~~next~~ 12 to 48 hours, according to the degree of injury ~~level~~, with secretion of plasma or ~~leaving of~~ blood fluids containing proteins, electrolytes and water.

The main ~~Principal~~ protein is albumin giving the ~~plasma~~ oncotic pressure (liquid retention) of the plasma and which moves to the ~~passing to the~~ extra-vascular space in the burn while retaining liquids in what is known ~~ich is called~~ as edema.

With the~~In~~ cell migration, due to ~~by~~ the increase in capillary permeability, ~~cells~~ specialized cells in injury response ~~ding to injuries~~ arrive: leucocytes (macrophages and neutrophils (~~circulation~~ immune white cells of the bloodstram) in charge~~d~~ of cleaning and disinfecting the~~is~~ area, a system of defense ~~system~~ against bacteria and elimination of dead cells ~~elimination~~).

Regarding ~~In respect to the~~ chemical substances, ~~of~~ dead cells, plasma and neutrophils produce some chemicals such as: ~~substances are produced:~~ euglobine, (capillary permeability), catecholamine, leucotaxine, bradykinin, k~~c~~allidine, kalliker~~c~~rein, histamine, serotonin and prostaglandins, all of which ~~substances~~ cause ~~ing~~ nervous stimulation, immune cell activity, vasodilatation, cell migration (chemotaxis) and other inflammation related changes.

BURN CLASSIFICATION

It is important to know how burns are classified ~~cation~~ according to their cu~~e~~taneous depth, etiology and extension.

Burns are classified according to diagnosis, treatment and prognosis parameters.

a) DEPTH

It is divided into three categories:

- First degree:

First degree – Superficial: only the stratum corneum or outer layers of the epidermis ~~or cornea layer~~ are affected. It is characterized by an erythema of red color, severe~~deep~~ pain, local heat, contact and air sensitivity and spontaneous healing in three to four days. It may cause ~~could produce~~ skin hyper-pigmentation. Sunburns are an~~A n~~ example of this type of burns~~is sun burn~~: healing occurs in a few days without scarring.

-Second Degree:

~~Second degree:~~

Superficial: partial or complete injury to the epidermis ~~injury~~ but with intact epidermal ~~is~~ attachments ~~annex~~ and ~~or~~ indentations, severe ~~deep~~ pain, erythema, phlyctene, fast capillary filling, ~~soft yet~~ skin still soft. E~~An e~~xamples of this type of burns are ~~is~~ scalds, which ~~heal~~ing in 8 days.

~~Deep~~: complete epidermis ~~complete~~ destruction (includinged ~~germinative~~ stratum germinativum) and part of the dermis, phflyctenaes, light ~~pale~~ rose tone, moderate pain (due to nerve~~ous~~ destruction), hardened and withered ~~cardboard-like~~ skin, slow capillary filling and slow ~~delay~~ healing originated from ~~beginning in~~ the attachments ~~annexes~~ (hairs and glands), and almost always

leaving a scare ~~is left~~. ~~An e~~Examples of the above are steam and flame burns ~~is steam or flame~~, ~~in~~ which ~~case~~ heal ~~regeneration occurs~~ in 16 days.

~~Third degree:~~

-Third degree:

There ~~is~~skin is entirely ~~a total~~ compromised ~~of skin~~, there is not cell regeneration, white~~-~~, insensible, withered~~cardboard-like~~, dry skin without edemas and may compromise ~~can involve~~ organs other ~~different~~ than skin, such as ~~for example~~in ~~,~~ electric, chemical and fire burns.

These~~is~~ burns always require ~~needed~~ specialized medical treatment~~attention~~.

First and second degree superficial ~~rface~~ burns undergo ~~have~~ spontaneously healing and are the main subject matter of application ~~principal object and applicability~~ of the composition in~~of~~ the present invention.

ETIOLOGY

Determining ~~ate~~ the origin of the burn is very ~~always~~ important to define the ~~lesion~~ intensity, treatment and prognosis of the injury.

Sun, biological, steam, flame and scalds burns produce the ~~cause~~ more superficial ~~face~~ burns, direct fire and chemicals burns cause intermediate ~~middle~~ burns and contact burns, deflagration and electric burns are the most dangerous.

CONSIDERATION AND DISPOSITION OF BURNS

-EXTENSIVE BURNS:

Critical burns:

These burns involve more than 25% of the body in adults and more than 10% in children and exceeding the second degree in depth. In addition to

~~These are burns involving more than 25% of an adult or 10% in children and with more than second degree depth. Apart from~~ local injuries such as necrosis, pain, vasculitis, edema, transudation ~~weating~~ and over-infection, there is a systemic compromise ~~implication in~~ which leads to immunological reactions, vasodilatation, exit of liquids ~~emergence~~ to the interstitial space, loss of protein ~~loss~~, necrotic ~~sis~~ residues, general sepsis and compromise of the ~~implication of~~ vascular and urinary systems ~~are presented~~. In these cases, patient treatment ~~s manage~~ is exclusively managed ~~de~~ by physicians and ~~in~~ hospitals with liquid, proteins and electrolytes replacement~~tesition~~, in-hospital care of wounds ~~hospital~~ and affected systems ~~care~~ (air~~borne~~ ways systems) and in ~~depth~~ cases of increased depth surgical treatments with grafts, flaps and reconstructive surgical ~~chirurgical~~ processes. These patients heal ~~are~~ slowly ~~healing patients~~ and may spend a long time ~~can be much time~~ in the hospital. ~~There are~~ Hhypertrophic scares, deformations and hair loss are some

of the possible sequelae. Patients who have ~~having~~ inhaled smoke are subject to ~~of~~ special care as this may lead to injury of ~~for production of~~ the airborne ways ~~illness~~, respiratory insufficiency and death~~ad~~. Antibiotic treatment of both the wound and in general is ~~Manage with antibiotics is~~ indispensable ~~both for the wound and in general because all~~as any ~~-~~patient with extensive burns suffers ~~of~~ over-infection.

SMALL~~LITTLE~~, MINOR AND SUPERFICIAL BURNS.

A superficial burn is understood as one that can be treated ambulatory at home or at a doctor's practice without complications and does not exceed 25% TBSA and superficial second degree in adults, and 10% superficial second degree in children. ~~It is considered a superficial burn those which can be ambulatory treated in house or in doctor's office without complications and not surpassing 25% sct and of second degree in adults, and 10% and second degree in children.~~

According to the parameters established, these are burns in which there is no hydroelectrolitic compromise of the body~~with no electrolytic implication of the organism~~, the immunological and vascular compromise ~~implication~~ is minor~~little~~, and there is no infection, ~~is presented with~~ except for ~~ion of~~ overlapping conditions. ~~aggregated situations.~~

In these~~is~~ cases, treatment is focused on ~~in~~ preventing an over-infection, loss of liquid~~losss~~, reducing ~~des~~inflammation of the zone, providing

comfortablenessoffering comfort, offering analgesia, cleaning the zone, covering the burn area and protecting it from the environment while the intrinsic healing processes occuract.

If a burn is smalllittle, shallow it is not depth and it is free of not complicationsed, the treatment consists of covering the zone, cleaning it, examininginspection it, and washing the zoneit, soothing take away the pain and debriding such zone, while it; preventing any over-infection and allowing permitting re-epithelialization and complete healing in a maximum period ofrom 3 to 5 days maximum. Use of ; analgesic, antibiotic substances and other local covering products is avoided as local coverare avoided. The novel composition subject matter of this invention has been designed for this local treatment of a burn.

This local treatment is the object of the composition of the present invention.

OBJECTIVES OF BURN TREATMENT

The oObjectives of the local burn treatment of burns are is protecting against infection and trauma, soothing diminishing the pain, reducing des-inflammation and accelerating the removal of e removing of dead tissue, while promoting methods that accelerate cicatrization. enhancing scaring. Superficial burns that epithelialize ing faster do so ing it with less scar.

Nowadays, the most common methodology for treating superficial burns includes generally the use of topical antimicrobial agents, . Ppreferably of silver sulfadiazine

(SSD). This drug was developed in the 60's and is effective for controlling ~~anti~~microbial growth in the burn as ~~while~~ the eschar separates. SSD has a hydrophobic molecule ~~making~~ that makes the application of the cream induce the ~~s~~ accumulation in~~of~~ significant amounts of proteinaceous exudates over the ~~in~~ wound surface.

These exudates are called PSEUDOESCHAR. It is necessary to undertake e~~E~~fforts ~~should be carried out~~ to remove ~~take away~~ this pseudoeschar, which ~~that~~ is a strong layer of material on the ~~in~~ burn surface, for ~~in the contrary, paradoxically paradoxically,~~ bacterial colonization can otherwise advance~~progress~~. Therefore the use of SSD ~~o~~in ~~in~~ burns should be accompanied by periodical surgical ~~requires surveillance and periodical chirurgical~~ debriding for removing the eschar and ~~the~~ accumulated proteinaceous necrotic residues.

The epithelialization ~~epithelization~~ process requires the burned zone to be clean and free of any debris, requiring in the case of SSD the removal of necrotic tissue, which ~~that~~ unfortunately can be extremely painful and stressing for the patient, and further requires the use of great doses ~~of~~ analgesic.

~~The~~ e~~E~~ndogenous ~~e~~ proteases are produced by various cells in a burned zone. These enzymes promote ~~enhance~~ the liquefaction and removal of ~~the~~ necrotic tissue; the devitalized protein~~e~~ residues must be removed in order to allow the epithelial cells to migrate and repair the surface of the burned ~~zone~~. C~~The co~~llagenase~~s~~ are intrinsically produced proteases (enzymes) ~~of intrinsic~~

~~production~~ that act exclusively on the collagen by ~~to~~ denaturizing ~~e~~ it and making it ~~more~~ easily ~~to be~~ degradable ~~ed~~ by less specific proteases.

For several ~~During~~ decades exogenous proteases ~~preparations~~ have been made to accelerate the debriding process of ~~the~~ burns and lesions ~~wounds~~ while increasing the local protein~~e~~ degradation rate and thus accelerating the epithelialization ~~epithelization~~ process. This translates ~~turns~~ into a reduction of intensity of the lesion, less care hours of the injury ~~decreasing the intensity of the injury or wound, less hours for taking care of the wound~~, and less discomfort for~~malaise of~~ the patient. E~~The~~ exogenous collagenase can be obtained from ~~in~~ an enzymatic preparation derived from the clostridium histolyticum bacteria.

PAIN AND TRAUMA OVER THE BURN OR SUPERFICIAL ~~RFACE~~ ABRASION

During the 12th annual congress of the European Wound Management ~~Handling European~~ Association held in Granada, Spain from ~~between~~ M~~m~~ay 23 to 25 of~~,~~ 2002, the attendants concluded that ~~for the~~ prevention of ~~the~~ misill treatment or trauma on a wound (dressing~~healing~~) and ~~pain~~ prevention of patient pain~~ng to the patient~~ were considered the ~~, the~~ most important elements relating ~~ed~~ to the care of an injury~~the wound should be taken into account~~. The removal of the dressings is the ~~a~~ biggest ~~-~~cause of pain and hence ~~therefore~~ a pain-free and non-trauma causing dressing ~~obtaining a dressing that eliminates or diminishes pain and trauma~~ is highly ~~a highly~~ desirable ~~ed characteristic~~.

FUNCTION OF PROTEOLYTIC ENZYMES ~~FUNCTION IN THE BURN~~ HEALING~~REPAIR~~

Injuries of all types, including ~~The wounds of all kinds, including~~ burns, all have something in ~~possess a~~ common ~~fact~~: they all produce the same ~~a~~ physiologic response. The severity of such response varies with the degrees or ~~and~~ types of wound.

~~The h~~Hyperemia is a physiologic response to trauma, which is followed by inflammation~~flare~~, a cicatrization pre-requirement, ~~that is a previous requirement to healing~~ and subsequently by ~~then causing~~ an edema, which usually delays healing~~curing~~. If the edema is too big~~excessive~~, it can delay ~~the~~ tissular~~e~~ metabolism thus increasing the possibility of ~~for~~ infection, ischemia and hypertrophic scars. Accordingly i~~I~~t is advisable ~~therefore convenient~~ to use ~~a~~ methods that reduce~~s~~ the edema.

An~~The~~ edema results from the accumulation of ~~represents a~~ excess liquids ~~excess~~ and cell residues ~~mainder~~ within the tissular spaces, while the ~~e gaps and its~~ elimination thereof depends on fluid ~~the liquid~~ drainage (for example, by applying pressure) and on the proteolysis, that is, ~~the~~ increased removal of ~~of the removal of the~~ protein residues ~~c remainder~~ by proteolytic enzymes. It has been proved (Tribuna Médica [Medical Tribune] ~~Medical Tribune~~ 354 1968) that ~~the~~ enzymes from the *carica papaya* reduce to a minimum the edema associated with inflammation ~~flare~~ in the injuries during the cicatrization process, a ~~wounds being~~

~~healed. Such~~ fact that is directly related to a substantial reduction ~~correlates directly with a significant decrease~~ or absence of pain.

CURRENTLY AVAILABLE

~~STATE OF THE ART~~ PRODUCTS FOR BURN TREATMENT

From homemade substances~~Starting with empiric substances~~, herbs, Aloe vera, mucilage etc.~~,~~ to ~~and continuing with~~ tannines, mercurial composition~~y~~, and topical antibiotics comprise ~~are~~ the wide range of ~~used~~ substances used to treat skin lesions ~~wounds~~ caused by burns~~ing~~ (or abrasions), which further proves the absence of an unanimous consensus in ~~simply demonstrates the lack of unity in criteria to~~ this~~at~~ respect.

Home ~~Empiric~~ treatments such as ~~with~~ coffee, onion, albumen ~~white of egg~~ and other ~~different~~ substances from ~~with~~ traditional knowledge are used in addition to ~~a~~ a medical care ~~handling~~ based on antibiotics and scab ~~crust~~ forming substances such as mercurochrome (chromium mercury) ~~chromium mercury~~ which have to be associated with analgesics and lubricants for the aforesaid lesions. ~~mentioned wounds.~~

Many other ~~different~~ products have been used with varying ~~average~~ results, such as cerium nitrate, i~~l~~odine (which c~~C~~auses pain), tannins, rifampycin, and a three-part combined ~~triconjugate~~ treatment consisting of ~~on~~ silver nitrate plus mercurochrome ~~chromium mercury~~ plus tannic acid. This treatment is ~~has an~~

antiseptically weak ~~tic weakness~~ and produces a scab that may be ~~can predispose to~~ bacteria culture prone.

The use ~~practice~~ of topic antibiotic therapy for burns was not designed to treat ~~the~~ recent superficial ~~rface~~ wounds, whose management target ~~ich handling management~~ is quite different. L~~The l~~ocal antibiotic therapy should be reserved ~~must be kept~~ for those clinical instances ~~cases~~ in which the ~~burn~~ sepsis of the burn, due to its extension, ~~magnitude~~ will become ~~can turn into~~ a major problem. A~~The~~ patient with a recent superficial ~~rface~~ burn will not benefit from the use of ~~by using~~ antibiotics.

S
~~s~~ome ~~OF THE~~ available products are:

-Mafenide: (sulfamilon) which is a methylated sulfonamide (sulfa group) effective against a wide range of bacteria ~~group~~, ~~in~~ particularly the *clostridium,* which can penetrate the scab and cause a metabolic acidosis.

-Silver nitrate: a~~A~~n inorganic salt having ~~a~~ poor injury ~~wound~~ penetration, helps remove~~ing~~ the scab, narrow ~~under~~ bacterial spectrum.

-Silver Sulfadiazine: c~~C~~omprises sulfadiazine and silver nitrate, penetrates the scab and is effective against the entire ~~burns~~ bacterial spectrum of burns.

-Gentamycin: uUsed against the *pseudomona aeruginosa*, possesses ~~a~~ quick bacterial resistance.

-Nitrofurazones: ~~They~~ have a limited ~~reduced~~ bacterial spectrum.

-Others: ~~The~~ butesiyn pPicrate, methatitanenate (zinc oxide, titanium dioxide, vitamin A), aloe vera, epidermiss growth factor (Cuban product) and other substances without therapeutic significance are found in the market.

-Use of proteolytic enzymes: The application of proteolytic enzymes on a burn wound with local sepsis is very useful ~~has a big importance~~ as it disrupts ~~the~~ coagulation, eliminates ~~the~~ accumulated proteinaceous material that "protects~~covers~~" the bacteria from ~~with the~~ antibiotic action and thus increases the antibiotic effectiveness, while ~~-~~preventing an ~~the~~ infection.

DESCRIPTION OF THE INVENTION

An ~~The~~ object of the present invention is providing ~~es~~ a topical composition for treating burns and ~~cootaneous injuries~~ sphacelus-causing skin injuries ~~sphacelus,~~ in connection with ~~from~~ each ~~every~~ one of the factors that produce a~~originating the~~ burn or su~~r~~perficial ~~face~~ abrasion: pain, for which the thickening ~~thickener~~ substance has been designed as a ~~was designed similar to a~~ second skin (thus producing ~~at is why it causes~~ analgesia), inflammation~~;~~ ~~flare~~, for which the proteolytic enzyme ~~was designed~~ having a potent ~~an~~ enzymatic debriding effect was designed, being th~~e~~ese the basic features ~~concepts~~ of gel.

Another objective of the present invention is to providing e a composition that besides containing the above-mentioned components, may it also can comprise contain other components effective on for secondary (non-primary) factors of the burns, such as adding an including antiseptic (chlorhexidine) in case an infection is suspected, urea for a better lubrication and an anesthetic (lidocaine) for the painful injuries wounds in adults and in particularly in children.

The sepsis of a the burned injury or burn is defined by Teplitz as: pPresence of bacterial organisms exceeding 100,000 colonies per gram of tissue gram in the burned tissue and which are actively that are invading the tissue underlying under the burned zone (artz Chap. 17, Pg. 250).

For During a short period of time after the occurrence of a burn, the wound remains generally sterile for up to an average of 48 hours in average, the subsequent later contamination comes from an the external sourcemedium, from the surrounding skin (sSaprophytesilous) and other sources such as respiratory sources and feces. It is important to recognize that the topical antibiotic therapy has been designed to control the sepsis of the burn and not for the regular outinary treatment of small little burns in which the sepsis is not athe problem.

After acquiring a Having clearly understanding of eod the concept of sepsis of a burned injury wound and the its possibility or not of its appearance or not during the initial in the burn's initial phase of a burn, the the use of an adequate therapy is then reasoned is rationalized. An overutilization of topical antibiotics may be

counterproductive ~~can produce the opposite of the desired effect~~ (overtreatment) for ~~due to the~~ saprophytile ~~ous~~ bacterial proliferation.

Microbiologically speaking, a~~A~~ few hours after the burn, ~~, microbiologically~~ a superficial ~~rface~~ bacterial colonization begins ~~is initiated~~ with a great variety of organisms, in particular positive gram cocci ~~u~~ (mainly the staphylococcusu~~u~~). This colonization is started from ~~by~~ the hair follicles and perifollicular tissue. After a period of 3 to 5 days the negative gram organisms become ~~are~~ predominant, which initiate an ~~the~~ invasion of the ~~burn underlying~~ tissues underlying the burn. There is a lymphatic d~~D~~issemination ~~through the lymphatic paths~~ to the blood stream ~~takes place~~. There are some factors that predispose to ~~bias the~~ bacterial over-infection such as ~~the~~ vascular destruction, which prevents the supply of ~~inhibiting the~~ nutrients and ~~apportion to~~ immune cells, ~~the~~ coagulation necrosis ~~of coagulation~~ that increases with the over-infection and the vascular necrosis. It has been widely proved that burns inhibit the immune response (vascular necrosis).

The topical antibiotic therapy does not sterilize the burn. ~~I, t just and~~ simply reduces the number of bacteria while trying to let ~~intending to allow~~ the immunological mechanisms of the host ~~to~~ control the infection.

Given that ~~As~~ flora in the burn ~~flower is~~ is not completely ~~absolutely~~ eradicated, the handling ~~effort~~ is intended to ~~addressed to~~ allow the replacement of the skin layer~~cootaneous cover~~.

When there is a bacterial colonization, the same ~~is~~ is initiated superficially, ~~on the surface~~ where there is dead or necrotic tissue and advances ~~deeps in~~ progressively in depth. The greater the extension, depth and elapsed time, the bigger the chances are of infection.~~Having wider affected area, wound deepness and longer time of occurrence, the greater the possibility of infection.~~ A~~The~~ age, nutritional and immunological condition of the individual, ~~being~~ exposure ~~ed~~ to the surrounding environment, persistent inflammation~~flare~~, location of the wound ~~location~~ and ~~wound~~ detritus on the wound are all important factors. A minor burn without any scab (detritus), clean tissues and isolated from the environment and without inflammation~~unflare,~~ provides ~~presents~~ the best defense against over-infection. It is impoertant to realize ~~ative to know~~ that a topical antibiotic therapy on a burn is specifically targeted to ~~directly addressed to~~ control the appearance of ~~the~~ sepsis on the burn and not as a regular ~~outine~~ treatment for~~of~~ small burns in which the infection is neither ~~ot~~ a threat nor a problem.

Currently ~~Today~~ there is a novel complementary approach different from the local therapeutic~~s~~ of burns~~,~~, named HYDROGELS, directed to provide ~~offer~~ comfort, analgesia and pain relief in a quick ~~short~~ time over ~~in~~ the burned area, in addition to an ~~besides an~~ anti-inflammatory ~~flare~~ and debriding effect. Such approach is neither ~~is not an~~ an antibiotic therapy, nor is it indicated ~~nor has been formulated~~ for scab removal. It relates to the formation of a ~~, the deal to form a~~ soft, clear and ~~mooth, transparent and~~ colloidal layer that isolates the area, thus ~~and thus,~~ preventing~~s~~ any ~~the~~ bacterial over-infection.

In line with ~~Under~~ the above concept, the new composition of the present invention was designed based on each one ~~from each one~~ of the factors that produces a ~~originated by the~~ burn or superficial ~~rface~~ abrasion: pain, for which the thickener substance acting as ~~was designed similar to~~ a second skin was designed (thus producing ~~at is why it causes~~ analgesia); inflammation~~flare~~, for which the proteolytic enzyme having a potent ~~was designed having an~~ enzymatic debriding effect was designed, being th~~e~~ese the basic concepts of the gel.

In addition it is also possible to add new components ~~One can also add new components~~ for ~~the~~ secondary factors (non- primary) of ~~the~~ burns, such as the addition of ~~adding~~ chlorhexidine in case an infection is suspected, urea for ~~a~~ better lubrication and anesthetic ~~(idocaine)~~ for ~~the~~ painful wounds in adults or ~~and in particular in~~ children.

The indications of the present invention are for the treatment of first degree injuries~~grade wounds~~, superficial second grade ~~superficial injuries~~wounds~~s~~, not infected, that are not ~~being~~ located in special areas and that cover ~~have~~ less than 25% of extension.

The composition of the present invention has a new clinical focus with the following characteristics: it is a clear film that reduces inflammation, relieves pain, isolates

the injured zone, features rheologic effect, prevents infection, is water absorbent and produces fast and efficient epithelialization. ~~forms a transparent film, antifraring, pain relief, isolates the wounded zone, has a rheological power, prevent infection, is water absorbent and produces a fast and efficient epithelization.~~

It is a ~~The composition is a~~ viscous clear ~~transparent~~ gel comprised in~~ntained in~~ a plastic tube designed to be applied and spread ~~ed~~ directly over~~n~~ the affected area. It is a new physiological stance ~~view~~ in topical ~~treatment~~, symptomatic and preventive treatment in the pathology of superficial and non-infected local avulsions or burns~~superficial and non-infected burns or local avulsions~~.

International articles refer to the debriding and anti-inflammatory ~~flaring~~ effect of ~~the~~ papain, whose ~~ich in~~ additional ~~of the~~ barrier ~~effect~~ or second skin effect is also used in the product.

In the design of the composition of the present invention, the combination~~mix~~, affinities and properties of the ~~described~~ substances described, being focused on the pathology for which they were prepared, result~~s~~ in a specific formula ~~adequate~~ for the treatment of the ~~ing~~ signs and symptoms exhibited in ~~that show in~~ burns or avulsions.

This new composition offers comfortable ~~when~~ used and ~~in its~~ application, mediate or immediate analgesia as well as ~~and~~ a proteolytic debriding effect. It forms a clear ~~Form a transparent~~ coating ~~layer~~ that allows a direct view of the wound and

has an apposite colloidal effect that exerts pressure isolating it effectively ~~immediately~~ from the surrounding environment.

The reduction in ~~decrease of~~ liquid loss, ~~the~~ easy handling and ~~the~~ mobility of the affected zone lead to an actual ~~addressed to an effective~~ prevention of over-infections and rapid tissue ~~to a fast~~ growth ~~of the tissue~~. ~~-~~The composition also offers other advantages such as its easy application and removal~~y application and removal~~, being free of adverse effects for the patient, being non-toxic ~~is no toxic to~~ for ~~the~~ tissues, pain-free in its indicated application~~does not produce pain when applied according to the indications~~, not staining or decolorizing the injury and having a ~~has an immediate analgesic effect, does not stain or bleach the wound and has~~ low cost.

MECHANISM OF ACTION

The composition creates a clear ~~transparent~~ colloidal film over the ~~wounded~~ injury ~~zone~~ covering the nerve~~eous~~ endings ~~terminals~~ (pain relief), isolating the injury from the external environment in order to prevent contact with ~~ing~~ harmful substances, maintaining the injury dry and~~a dried zone and~~ applying pressure (apposite effect)

in order to create a medium allowing ~~a~~ fast and reliable cell regeneration; while the enzymatic action reduces ~~the~~ inflammation, debrides and cleans the zone.

The market of ~~the available~~ products available for handling burns and superficial abrasions is somewhat ~~uncertain~~vague: ~~, as they are~~ substances that are~~were~~ not designed to follow the course of the physiopathology ~~course~~ of these wounds and that simply ~~they just~~ refresh, ~~and~~ act as topical antibiotics or provide ~~give~~ temporary relief without being tailored specifically ~~for in~~ pain relief and anti-inflammation~~flare~~.

The basic concept underlying ~~of~~ the composition of the ~~minute~~ current ~~present~~ invention is to ~~that of~~ treating with ~~with~~ each one of its ~~their~~ components all the issues relating to ~~aspects of~~ the physiopathology of burns:~~;~~ the pain is produced by ~~happens due to the~~ nerve endings ~~ous terminal~~being left exposed ~~exposition~~ and the gel ~~of the invention~~ creates an external clear ~~transparent~~ layer that covers the injury ~~skin~~ while the skin undergoes the natural and normal epithelialization process ~~takes place~~. This coating ~~Said layer~~ helps this~~at~~ process to be concluded ~~develop~~ faster as it provides a more suitable condition and ~~makes the~~ medium ~~and conditions more adequate~~ (cleanliness~~s~~, debridation~~es~~, protection~~s~~).

The inflammation occurs due to the ~~injury reacting~~ physiological processes of reaction to injury (vasodilatation, cell migration, release of active substances ~~liberation~~ such as histamine and serotonine), and the effectiveness of ~~and the~~

~~efficiency of the~~ papain and the enzymes in the topical ~~are proven to act well in the topical~~ treatment and handling of the dermal ~~ic~~ inflammatory processes has already been proved.

Accordingly, ~~Therefore,~~ it was found that the combination of protecting barrier-enzymatic substances in search of a new handling in the ~~protecting substances looking for a new management~~ treatment of ~~in the~~ burns and superficial abrasions ~~treatment~~ was ideal ~~to said treatment~~.

COMPONENTS OF THE COMPOSITION

a. ~~The p~~Papain. It ~~i~~s a plant proteolytic enzyme ~~extracted~~ from the *Carica papaya* that hydrolyzses peptidic, amidic and esteric bonds of ~~the~~ proteins.

Its properties are having a good proteolytic activity, good thermo-stability, being~~are~~ thermo-soluble, anti-inflammatory and exhibiting ~~have~~ a debriding effect. In particular, it has a proteolytic activity from ~~between~~ pH 3 to ~~and~~ 9, a wide range of thermo-stability (up to 70° C), is poor in germ ~~s~~ content and dissolves easily in water, and has a high effectiveness ~~ity~~ in viscous solutions.

P~~The p~~apain has many ~~applications and~~ uses: as ~~is a~~ digestive substance that promotes or substitutes other digestive enzymes, used as an ~~is~~ antihelminthic by destroying the protein~~e~~ cuticle of intestinal worms, and in the leather, tobacco and ~~,~~ textile industries and as a ~~s and~~ meat softener. ~~smoother industries. In~~N wounds and burns it provides ~~presents~~ a proteolytic activity on dead tissues, without

attacking ~~affecting the~~ live tissues, causing ~~an~~ enzymatic debridement ~~scrubbing~~ and an optimal cicatrization~~healing~~. It has an inherent anti-inflammatory effect and it may be ~~is able to be~~ combined with certain antibiotics.

It is also used in biochemistry in breaking ~~the~~ bonds and ~~to~~ determininge chemical structures of other proteins (as in the determination of human Ig-G).

~~The p~~Papain is a protease that catalyzes ~~the hydrolysis of~~ esters and peptides hydrolysis. The main ~~most important~~ amino acids comprising the same ~~ed in it~~ are: tryiptophan, tyrosine, phenyl-alanine, histidine and arginine.

~~The p~~Papain is used ~~preferably~~ in the composition of the present invention preferably in a~~the~~ range from ~~of~~ 0.2 to ~~and~~ 5 % by weight of the composition, preferably in an amount of ~~around~~ 0.5% by weight of the composition.

b. C~~The c~~arboxymethyl-cellulose. This component is a synthetic resin derived from the ~~the~~ acrylic acid. It ~~,~~ is a thickener, emulsifier and interface coalescent (consistence). It provides the following features to the ~~s properties in the~~ composition of the present invention ~~are~~:

-Protecting barrier, or second skin that isolates the wound while the papain acts.

-Provides ~~Gives~~ the necessary stabilization as well as ~~ty,~~ filmogenous and ~~producing agent and~~ physiologically inert agents.

-Good antibacterial barrier.

This component is a well-known product and it is used in several ~~various field of~~ industrial production fields such as: foodstuffs, textiles, detergents, cosmetics, paints, adhesives, ceramics, toothpaste, leather, etc. It ~~This~~ is a cellulose-derived anionic polymer with ~~and hold~~ the following properties:

a. Dissolves ~~very~~ easily in cold or hot water.

b. Acts as a thickening agent, suspension agent and suspension stabilizer.

c. Retains ~~Hold in the~~ water thus contributing to keep dry ~~with the dryness of~~ the underlying wound.

d. Acts as a filmogenous ~~producing~~ agent that is oil, fat and organic solvents resistant.

e. Acts as binder ~~ing~~ and as colloid protector.

f. Is a rheological ~~al~~ control agent.

g. ~~It i~~Is physiologically inert, an essential property for the ~~searched~~ effect sought.

The CMC solution does not coagulate ~~turn solid~~ when heated~~with heating~~, as there is ~~it~~ only a reduction in ~~diminishes~~ its viscosity when the temperature exceeds ~~increases above~~ 40°C. It ~~,~~ has a high resistance to microbiologic attacks and when stored for long periods of time, the ~~subjected to long term storing the recommendation is~~ use of preservatives is recommended to avoid viscosity reduction ~~the decrease in viscosity~~ and ~~its~~ degradation. It has a broad range of

~~has also~~ stability, ~~within a wide range~~ from pH 4 to pH 9, being preferred a neutral pH ~~the preferred pH neutral~~.

The preferred range of use of this component is from ~~between~~ 1.0 to 4 % by weight of carboxymethylcellulose gel and the~~is~~ gel carboxymethylcellulose is present in a range from~~of~~ 71.5 to 77.5 % by weight of the composition ~~of the present invention~~.

c. CARBOPOL. This a high molecular weight synthetic resin ~~with a high molecular weight~~, polymerized with a hydrophobic monomer, obtaining a cross-linked polymer ~~with crosslinked chains~~ extracted from the acrylic or polyacrylic acid. Its ~~His~~ chemical name is carboxypolymethylene.

It is mainly used as a thickener and emulsifier, its function is maintaining the homogenization of the preparations, stabilizing emulsified systems against sedimentation or separation, absorbing the respective interface (oil-water). ~~The~~ CARBOPOL coalesces rapidly the application of the product ~~giving it consistence~~ with its emulsion ~~when~~ stabilization ~~ing~~ and thickening effect by giving it consistency ~~the emulsions~~.

Its main features ~~advantages~~ are:

a. Forming ~~it forms~~ a barrier that protects the skin from new potential external irritants.

b. ~~it~~ Cleaning ~~s nastiness~~ and removing ~~es the~~ undesired oily substances.

c. Distributing it uniformly distributes the composition preparation overn the skin.

d. Ait acceleratinges the stabilization of the compositionpreparation.

e. Being its stable ility for two years at room temperature.

f. Requiring low concentrations of CARBOPOL are needed to obtain get the desired effect.

g. it eEliminatinges the need for of emulsifying ier soaps.

h. Being it is clear translucent and does not producing e any skin coetaneous irritation.

i. In the event of coming in contact if occasionally contacts with the eyes, it may can cause minor irritation.

j. Nnot poisonous when ingested.

There are many types of carbopols, the most important are Carbopol 941, Carbopol 940, Carbopol 934, Carbopol ultrez 10, Carbopol etd-2020. Carbomer polymers have been used for rheological control (structuring e constructive agents) in lotions, creams and gels. Polymer molecules have thea unique abilityability ofto increasinge the viscosity thickness of liquids in which they are dissolved (dispersed), even in including very wet- concentrations. This is due to because of the volume inous expansion ability capacity (water absorption) of carbomer microgels.

The viscosity increase Polymer capacity of a polymer to increase the thickness depends on its "intrinsic viscosity". The unit employed to express "Intrinsic

viscosity" is ~~expressed in~~ dL/g. Factors that affect intrinsic viscosity of carbomer polymer are: pH, types of electrolytes and~~,~~ ion~~s~~ concentration.

Microgel particles in polymers increase the viscosity ~~thickness~~ of a solution by means of two mechanisms: 1) increasing viscosity in a direct ratio to the polymer´s swelling ~~according to the polymer swelling,~~ and 2) increasing viscosity by microgel stiffness.

The preferred range of ~~for~~ use for this component in the composition is from ~~between~~ 1~~,~~5% to~~and~~ 2~~,~~5% by weight of Carbopol gel, and ~~the amount of~~ Carbopol gel is present in an amount from ~~between~~ 22-28% by weight of the composition.

Optionally, the composition comprising the three components a., b. and c. mentioned above ~~described~~ may also include an analgesic in order to ~~with the aim to~~ bock ~~the~~ nerve~~ous~~ conduction, when ~~they are~~ locally applied~~administered~~. Lidocaine is the most stable local ana~~e~~sthetic~~,~~ and consequently the most commonly used ~~therefore, the most used~~ nowadays. It is currently used in ~~local~~ anaesthe~~t~~tic solutions for topical application and for mucous membranes, and also as injectable anaesthetic, infiltration anaesthesia, and in cardiology as a modifier of cardiac rhythm. It is used in the ~~a~~ composition in a range varying from 1% to 5% by weight of the composition.

EXAMPLES OF COMPOSITIONS FOR DIFFERENT TYPES OF APPLICATIONS

EXAMPLE 1

In a first embodiment, the composition of the present invention is prepared in three steps:

a) First, a CARBOPOL gel is prepared, which is present in the composition in 25% by weight.

b) Secondly, the carboxy-methylcellulose gel is prepared, which is present in the composition in 74,5% by weight.

c) Finally, papain is added in an amount of 0,5% by weight to the composition.

a. CARBOPOL GEL. This gel is prepared according to the following composition:

Carbopol,	2.00%
Triethanolamine,	2.23%
Distilled Water	95.77%.

Total CARPOBOL gel 100,00%.

b. CARBOXIMETHYLCELLULOSE GEL. This gel is prepared according to the following composition:

~~3,00%~~ Carboxymethylcellulose Sodium 3.00%

~~0,50%~~ Propyl Parebene~~,~~ 0.50%

~~0,50%~~ Methyl Parabene 0.50%~~,~~

~~96,00%~~ Distilled Water 96.00%.

Total ~~amount of~~ carboxymethylcellulose gel~~,~~ 100~~,~~00%.

c. ACTIVE PRINCIPLE. PAPAIN

~~0,50%~~ PAPAIN~~.~~ 0.50%

Formula of standardized manufacturing lot~~batch for manufacturing~~: 5~~,~~000 g

RAW MATERIALS AMOUNT

PAPAIN 25 grams,

CARBOPOL GEL 1~~,~~250 grams,

CARBOXYMETHYLCELLULOSE ~~GEL~~ SODIUM GEL 3~~,~~725 grams.

TOTAL AMOUNT RAW MATERIALS 5~~,~~000 grams.

According to the abovementioned ~~e established~~ percentages, ~~next are~~ the ~~necessary~~ amounts ~~-~~necessary for manufacturing the composition subject matter of the present invention are detailed below:

a. CARBOPOL GEL: 1~~,~~250 g

RAW MATERIAL _____AMOUNT

Carbopol _____25.0 grams,

Triethanolamine _____28.0 grams,

Distilled water _____1,198.0 grams

Total Raw Materials _____1,250 grams

b. CARBOXYMETHYLCELLULOSE SODIUM GEL: _3,725 grams.

Carboxymethylcellulose Sodium _____112.0 grams,

Propyl Parabene _____19.0 grams

Methyl Parabene _____19.0 grams,

Distilled Water _____3,576.0 grams

c. PAPAIN _____25 grams

2. Example of the manufacturing process:

~~s:~~

a. CARBOPOL GEL

1. Select ~~Take~~ a 2 kg capacity stainless steel ~~capacity~~ container.

2. Pour the distilled water in the stainless steel container.

3. Slowly add the triethanolamine ~~into the container~~.

4. Start the stirring process with a stainless steel stirrer~~haker~~.

5. Keep ~~on~~ stirring while ~~slowly~~ the c~~C~~arpobol is slowly added.

6. Pour into a~~the~~ mixer, stir~~ring~~ at minimum speed for about 15 min. until completely dissolved ~~ution is complete~~ and a clear ~~transparent~~ gel is obtained.

b. CARBOXYMETHYLCELLULOSE GEL

1. Select ~~Take~~ a 5 kg capacity stainless steel ~~capacity~~ container.

2. Pour the distilled water in the stainless steel container.

3. Slowly add the carboxymethylcellulose ~~into the container~~.

4. Start the stirring process with a stainless steel stirrer~~haker~~.

5. Keep on stirring while slowly adding the propyl paraben~~e~~.

6. Keep on stirring while adding the methyl paraben~~e~~.

7. Warm this ~~e~~ mixture until reaching a temperature of ~~at~~ 50 to 60°C, while constantly stirring.

8. Stop heating and keep stirring until the mixture reaches room temperature.

9. Pour into the mixer and ~~,~~ stir~~ring~~ at minimum speed until the mixture reaches a temperature of 17°C.

c. PAPAIN

1. In athe stainless steel container pour the CARBOPOL GEL.

2. Slowly add the CARBOXYMETHYLCELLULOSE GEL into the container.

3. Start the stirring process with a stainless steel stirrerhaker.

4. Keep on stirring while slowly adding the PAPAIN is added.

EXAMPLE 2

In a second embodiment, a composition having the following next components is provided:

a. First substance: it is Aa proteolytic enzyme, in this case particularly the papain derived from *cCarica papaya*, whose ich dedriding healing and anti-inflammatory advantages characteristics are used for the treatment of injurieswounds.

b. Second substance: CARBOPOL.

c. Third substance: carboxymethylcellulose sodium salt.

d. Forth substance: local anaesthetic drug.

The composition or quantitative formula of from the product is prepared in three steps and it is described as follows, according to the next description:

1. 25% CARBOPOL GEL _____ 25%

2. 72,5% CARBOXYMETHYLCELLULOSE GEL ____ 72.5%

2. 2.0% LIDOCAINE_____ 2.0%

3. ~~0.5%~~ PAPAIN. _____ 0.5%

The composition of the present invention is prepared in three steps:

a) A ~~First,~~ CARBOPOL gel is first prepared, which comprises 25% by weight of ~~present in~~ the composition ~~in 25% by weight is prepared~~.

b) Then, preparation is made of the carboxymethylcellulose gel, which comprises 72.5% by weight of ~~present in~~ the composition ~~in 72,5% by weight is prepared~~.

c) Finally, papain and lidocaine are added in amounts of 0.5% and 2%, respectively, by weight~~, based on the total weight~~ of the composition~~, of papain and Lidocaine, respectively, are added~~.

a. CARBOPOL GEL. This gel is prepared according to the next composition:

Carbopol _____ 2.00%,

Triethanolamine _____ 2.23%,

Distilled Water _____ 95.77%.

Total ~~amount of~~ CARBOPOL gel _____ 100.00%

b. CARBOXYMETHYLCELLULOSE GEL. This gel is prepared according to the following ~~next~~ composition:

Carboxymethylcellulose Sodium _____ 3.00%,

Propyl Parabene _____ 0.50%,

Methyl Parabene _____ 0.50%,

Distilled Water _____96.~~,~~00%.

Total carboxymethylcellulose gel _____100.00%

c. ACTIVE PRINCIPLE. PAPAIN

Papain _____0.~~,~~50%.

d. AN~~A~~ESTHETIC.

Lidocaine~~-~~_____2.00%.

2. Example of the manufacturing process:

a. CARBOPOL GEL.

1. Select ~~Take~~ a 2 kg capacity stainless steel ~~capacity~~ container.
2. Pour the distilled water in the stainless steel container.
3. Slowly add the triethanolamine ~~into the container~~.
4. Start the stirring process with a stainless steel stirrer~~haker~~.
5. Keep on stirring while slowly adding the c~~C~~arbopol ~~is added~~.

6. Pour into the mixer, stirring at minimum speed for about 15 min until dissolution is complete and a clear transparent gel is obtained.

b. CARBOXYMETHYLCELLULOSE GEL CARBOXIMETILCELULOSA GEL

1. Select Take a 5 kg capacity stainless steel capacity container.
2. Pour the distilled water in the stainless steel container.
3. Slowly add the carboxymethylcellulose into the container.
4. Start the stirring process with a stainless steel stirrerhaker.
5. Keep on stirring while slowly adding the propyl parabene is added.
6. Keep on stirring while the methyl parabene is added.
7. Warm this mixture until reaching a temperature of 50 to 60°C, while constantly stirring.
8. Stop heating and keep stirring until the mixture reaches room temperature.
9. Pour into the mixer and stir at minimum speed until the mixture reaches a temperature of 17°C.

Warm the mixture at 50 to 60ºC, constantly stirring.

8. Stop heating and keep stirring until the mixture reaches room temperature.

9. Pour into the mixer, stirring at minimum speed until the mixture reaches a temperature of 17º C.

c. PAPAIN AND LIDOCAINE

1. Pour the carbopol gel into athe stainless steel container.

2. Slowly add the carboxymethylcellulose gel into the container.

3. Start the stirring process with a stainless steel stirrerhaker.

4. Keep on stirring while papain and lidocaine are slowly added.

Preparation of the composition of the present invention with chlorhexidine and urea is similar to the above and follows the same parameters ofas the procedure above described above.

EXAMPLE 3

COMPARATIVE CLINICAL RESULTS ARE COMPARATIVE WITH EXISTING THE PRODUCTS ALREADY EXISTING.

A cClinical evaluation of the product was made, which contained ere datum of the patient data, a brief anamnesis, a description of the injury wound and a time monitoring time chart picture with the variables PAIN, INFLAMMATION and DEBRIDING HEALING EFFECT.

In additionFurthermore, the presence of overinfections was investigated, which and the result was negative.

STUDY GROUP: 44 Patients having ~~diagnosed with~~ a burns or avulsion diagnostic and ~~that fulfil~~ meeting the requirements to apply the composition of the present invention were selected.

ADMINISTRATION SCHEME, DOSES, ROUTE AND FREQUENCY

The product under study is ~~exclusively~~ for cu~~o~~taneous application only, and once an ~~the~~ injury ~~wound~~ has been made~~occurred~~, its application is made in topical ~~of topic~~ dosage~~s~~~~es~~ every ~~is distributed each~~ 2 hours, modifiable once ~~according to~~ the ~~process of~~ skin renovation process is noted.

The c~~C~~omparative study was conducted with ~~of~~ the composition of the present invention and ~~was made with~~ aloe vera (a substance derived from the aloe vera plant~~sabila~~, recommended and advertised ~~publicized~~ for handling burns and having a similar appearance to the ~~similar~~ composition of ~~to~~ this ~~e present~~ application), both in gel presentation~~ackaging~~.

No~~ne~~ antibiotic cream was used in this study, since the object was not infected injuries ~~wounds~~ or areas already subjected to a ~~where the process of~~ bacterial growth process. ~~ing has occurred are not the objective.~~

Most ~~of the wounds~~ treated injuries varied from ~~fluctuated in an extension between~~ 1 to ~~-~~10%~~,~~ in extension, excluding some patients who were applied ~~that received~~

the present composition in extensive ~~spread out~~ burns of up to 30%. All injuries ~~the wounds~~ were of first and second grade according to their depth, which are those likely to heal ~~capable to improve~~ with these products.

No~~t~~ important complications were observed, although ~~and~~ some burns treated with Aloe Vera frequently followed an ~~continued the normal~~ infectious development ~~process that is common~~ in these injuries~~cases~~.

The p~~P~~roducts were applied according to the following ~~next~~ evaluation times:

- 0 Hours: Initial clinical evaluation.
- 6 Hours: during this period of time, the symptoms for these specific injuries are felt ~~of these specific wounds are~~ stronger.
- 24 Hours: At this time~~during this period of time~~ all first and second degree burns and covering small areas have a stabilized ~~,~~ symptomatology under a natural process and their injury resolution starts.~~of all wound caused by burns of first and second grade in small areas, finds stability starting its resolution during the natural process.~~
- 72 Hours: This type of injuries under a natural and regular development are in recovery, missing a high percentage of signs and symptoms.

~~natural development of this kind of wounds is in the recovery sep, with the absence of most of the symptoms and signs.~~

~~PERFORMANCE ANALYSIS WITH~~ ALOE VERA RESULT ANALYSIS:

As an adjuvant ~~helper~~ in the initial symptomatology, it refreshe~~ns~~ and soothes and as part of the ~~, calms and, as a part of the~~ general measures, it has some level of efficiency without being the ideal product in connection with ~~reference to~~ the evolution thereof.

In general, patients believe ~~that~~ the product to be "refreshinge~~ns~~, ~~is~~ good" and to aid ~~helps~~ in the initial comforting ~~of~~ the wound, ~~mean~~while during the following hours~~in subsequent hour~~, it does not have any kind of c~~C~~linical incidence, all related with the natural evolution of the injury~~wound~~, its extension, depth and localization. 50% of the patients consider the product to be ~~is~~ good, between ~~between~~ good and excellent 10%, and average ~~regular~~ 12%.

~~In general,~~ Physicians' opinions ~~medical concepts~~ are generally good~~,~~ 52%, improves patient's comfortableness ~~improves~~, excellent 10% and~~,~~ 30% prevents greater inflammation ~~remains the same, 30%~~. Most ~~of~~ medical reports declare persistent ~~ce of~~ discomforts related to pain and inflammation, and an aqueous appearance ~~characteristic~~ of the Aloe.

EVOLUTION OF PAIN:

Most of the patients had severe ~~agonizing~~ pain at the time of the initial evaluation.

After 6 hours of starting the handling with ~~before~~ Aloe~~'s application~~, the pain had substantially subsided~~intensity of pain was of less intense~~, although some patients still had intense pain (13%.)

After 24 hours ~~later~~: some patients still report ~~between~~ moderate to mild pain and ~~and minor pain and, but~~ 70% without ~~without~~ pain.

After

72 hours ~~later~~: 5% of the patients with moderate~~d~~ pain, 18% mild ~~minor~~ and 77% without pain.

EVOLUTION OF THE INFLAMMATION:

Most of the injuries ~~wounds~~ were small.

After 6 hours ~~later~~: One~~A~~ patient has severe inflammation and 33% have~~ve~~ ~~mild minor~~ inflammation.

After 24 ~~hours later~~ hours: 30% remain with mild inflammation ~~30% of the group still have minor inflammation~~ and moderate in ~~,~~ almost 50% of the group ~~moderated~~.

After 72 hours: ~~later,~~ 36% of the patients still report~~s~~ mild ~~minor~~ inflammation.

CLEANSING EVOLUTION ~~OF THE CLEANING~~:

Not significant.

ANALYSIS OF RESULTS WITH THE COMPOSITION OF THE EXAMPLE 1:

The opinion rendered ~~concept emitted~~ by the patients with respect to the product being in ~~is in~~a superlative and excellent ranking ~~grade~~ is ~~in~~ 48%, good 42%, 10% of patients di~~d~~o not provide any opinion~~emit a concept~~, there were~~are~~ no~~t~~ average rankings ~~regular concepts~~. The study reports ~~In~~ some cases~~,~~ of mild discomfort ~~its reported minor annoyances at the time of the~~ upon application~~,~~ and ~~a~~ fast pain relief ~~of the pain~~ throughout ~~during~~ the ~~whole~~ study. ~~The e~~Epithelialization and ~~remove the~~ deinflammation occur after ~~in~~ a short period of time.

The physicians' opinions ~~Medical concepts are equally~~ also are in superlative ranking~~grade~~, very good and excellent 32%~~5~~, and good 46%; magnificent analgesia, efficient product, easy to handle product and used in wider and more serious injuries. ~~area~~

EVOLUTION OF THE PAIN WITH THE COMPOSITION OF EXAMPLE 1:

After 6 hours ~~hours later~~: 35% of the patients have severe ~~intense~~ pain at time ~~he hour~~ zero, and six hours later, this percentage is reduced to ~~diminish to~~ 3%.

After 24 hours ~~later~~: pain is mild ~~minor~~ and~~,~~ 87 % do not have any pain.

After 72 hours ~~later~~: o~~O~~nly 3% of the patients have a mild degree ~~minor grade~~ of pain and~~,~~ 89% do not report pain.

EVOLUTION OF THE INFLAMMATION WITH THE COMPOSITION OF EXAMPLE 1:

After 6 ~~6~~ hours ~~later~~: one patient with severe ~~intense~~ inflammation, 35% with mild ~~minor~~ inflammation and~~,~~ 46% without inflammation.

After 24 hours ~~later~~: o~~O~~nly one patient reports severe ~~intense~~ inflammation, most ~~of them~~ (78%) do not have inflammation.

After 72 ~~hours later~~: 2% report mild ~~moderated~~ inflammation and~~,~~ 85% do not have inflammation.

These results confirm the effectiveness of the product for ~~on~~ pain an inflammation. As it may ~~can~~ be noted~~seen~~, the compositions subject matter of the present invention have superior analgesic, protective, debriding~~healing~~, and anti-inflammatory effects over those of the ~~in reference to all of the previously known in the~~ S~~s~~tate of the A~~a~~rt.

The above examples should not be construed as limiting ~~of~~ the scope of the present invention and the scope of the same is determined by the claims provided below~~appended hereto~~.

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